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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,716	01/28/2002	Kenji Asano	0230-0160P	3342
2292	7590	04/06/2005	EXAMINER YAO, LEI	
BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 04/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/856,716

Applicant(s)

ASANO ET AL.

Examiner

Lei Yao, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 March 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 is/are pending in the application.
- 4a) Of the above claim(s) 3 and 4 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 2 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
- Paper No(s)/Mail Date 3-10-05

- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION***Election/Restrictions***

Applicant's election with traverse of Group I in the reply filed on 3/10/2005 is acknowledged. The traversal is on the ground(s) that special technical feature is not obvious over the prior arts.

Applicants argue that the special technical features of the present invention is that demonstration for the first time that the extract of *Lentinus edodes* mycelium of the invention actually has an ability to activate LAK cells both in vitro and in vivo and that the in vitro LAK activity enhancing effect of the extract is parallel to that in vivo. Applicants further argue that the restriction is improper because neither Yamamoto et al., nor Liu et al., disclose or suggest the claimed technical feature.

These have been considered, but not found persuasive. The technical feature of group I is in vitro method of whether a compound or composition has LAK activity enhancing effect by the claimed active steps of (a) through (c), and the claimed invention in group I is not limited to a method involving *Lentinus edodes* mycelium. Rather, the claimed method involves any "screening material", not just *Lentinus edodes* mycelium. Note the claim limitation of claim 1 step (a) to (c), the claimed method is also anticipated by Mule et al., (1991, see the art rejection below).

According to PCT rule 13.2, unity of invention exists only when the same or corresponding technical feature is a contribution over the prior art. Yamamoto et al., (Biosci Biotech Biochem, vol 61, p1909, 1997) teach a material from *lentinus edodes* mycelium. Yamamoto et al., also teach the enhancing a cytotoxicity of lymphocytes treated by an extract of *lentinus edodes* mycelium. Thus, the special technical feature, an extract of *lentinus edodes* mycelium, is not a contribution over the prior art according to the teaching of Yamamoto et al. and the unity of inventions is lacking. For this reason, the restriction requirement is deemed to be proper and is adhered to. The requirement is therefore made **FINAL**.

Claims 1-4 are pending. Claims 3-4, drawn to non-elected inventions, are withdrawn from consideration. Claims 1-2 will be examined on the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Mule et al., (Current Protocol in Immunology, unit 7.7, page 7.7.1-7.7.5 and unit 7.18, page 7.18.1-7.18-7, 1991).

Claim 1 is broadly interpreted as drawn to a method of screening whether a compound or composition has LAK activity by (a) isolating peripheral blood to prepare lymphocyte fraction, (b) adding the product or the composition to be screened to the isolated lymphocyte fraction, and then (c) measuring the LAK activity of the lymphocytes with the added product or composition, and compare the activity with the control sample that does not contain the product or composition.

After consulting the specification at page 9, lines 2-4, "As used herein, screening materials refer to materials used for testing in vitro the LAK activity-enhancing effect obtained by in vivo administration", the Office considers that the limitation "a screening material of the present invention" in step (b) of claim 1 is not limited to *Lentinus edodes* mycelium. Also note claim 2 further limits "a screening material" of the base claim to be an extract of *Lentinus edodes* mycelium, which indicates that the "screening material" of the base claim is broader than *Lentinus edodes* mycelium.

Mule et al., discloses (a) isolating peripheral blood to prepare lymphocyte fraction from human blood (protocol on page 7.7.1-7.7.3), (b) adding IL-2 as "screening material" to the isolated lymphocyte fraction to activate LAK cells (page 7.7.2, line 34- 36), and (c) measuring the LAK activity of the lymphocytes and comparing the activity of LAK cells treated with screening material, IL-2, with the control sample that does not contain IL-2 (protocol on page, 7.18.1-7.18.4). Mule et al., disclose that cytotoxic

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activity of lymphocytes is enhanced after the lymphocytes are treated with IL-2 compared to the control of lymphocyte fraction without treatment (page 7.18.5, table 7.18.1).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mule et al., (Current Protocol in Immunology, unit 7.7, page 7.7.1-7.7.5 and unit 7.18, page 7.18.1-7.18-7, 1991) and further in view of Yamamoto et al., (Biosci Biotechno Biochem, vol 61, p1909-1912, 1997).

Claim 1 is broadly interpreted as drawn to a method of screening whether a compound or composition has LAK activity by (a) isolating peripheral blood to prepare lymphocyte faction, (b) adding the product or the composition to be screened to the isolated lymphocyte fraction, and then (c) measuring the LAK activity of the lymphocytes with the added product or composition, and compare the activity with the control sample that does not contain the product or composition. Claim 2 embodies the claim 1, wherein the screening material is an extract of lentinus edodes mycelium.

Mule et al., teach (1) isolating peripheral blood to prepare lymphocyte faction from human blood (page 7.7.1-7.7.3), (2) activation of the isolated lymphocyte fraction to LAK cells by IL-2 treatment (page 7.7.2, line 34-36), and (3) measuring the LAK activity of the lymphocytes and comparing the activity of IL-2 activated LAK cells with the control sample, which are not treated with IL-2 (protocol on page, 7.18.1-7.18.4).

Mule et al., do not teach that cytotoxicity of lymphocytes can be induced by an extract of Lentinus edodes mycelia.

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Yamamoto et al., teach that cytotoxicity of lymphocytes, specifically NK cells, induced by an extract of culture medium of *Lentinus edodes* mycelia. Yamamoto et al., first teach how to prepare fractions from the extract of *Lentinus edodes* mycelia (page 1909, col 2, paragraph 1). Yamamoto et al., then teach a cytotoxicity assay against fibrosarcoma cells using lymphocytes, specifically NK cells, treated with a fraction of the extract of *Lentinus edodes* mycelia, JLS-18. Yamamoto et al., further teach that the extract of *Lentinus edodes* mycelia, specifically a fraction JLS-18, is effective activator of lymphocytes for their cytotoxicity against tumor cells (page 1911, col 1, paragraph 2 and figure 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teaching of Yamamoto et al., on the activation of NK cells by an extract of *Lentinus edodes* mycelia with the teaching of Mule et al., on the lymphocyte fraction isolated from blood to prepare the LAK cells and measure a screening material, specifically, an extract of *Lentinus edodes* mycelia, to have a LAK activity-enhancing effect. One of skill in the art at the time of invention would have a reasonable expectation of success in determination of LAK activity-enhancing effect in lymphocytes treated with an extract of *Lentinus edodes* mycelia.

One of ordinary skill in the art would have been motivated to make and use the claimed invention, that is, the LAK activity-enhancing effect is induced by an extract of *Lentinus edodes* mycelia, because Yamamoto et al., teach that an extract of *Lentinus edodes* mycelia, JLS-18, is an effective activator of lymphocytes for their cytotoxicity against tumor cells (page 1911, paragraph 2) and an extract of *Lentinus edodes* mycelia, JLS-18, could activate lymphocytes and might be effective on the patients with hepatitis and AIDs through such immunopotentiating activity and useful for the therapy of these disease (page 1912, paragraph 2).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-4.30pm Monday to Friday.

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Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao, Ph.D.
Examiner
Art Unit 1642

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MISOOK YU
PATENT EXAMINER